ATTORNEY DOCKET NO.: 078883/0146
APPLN. NO.: 10/088,076

REMARKS

Applicants respectfully request formal examination of this application.

Applicants have amended the specification to identify amino acid sequences according to their SEQ ID NOs. As the amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

If there are any fees due in connection with the filing of this Preliminary Amendment, please charge the fees to our Deposit Account No. 19-0741. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

By _____

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Date July 19, 2002
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MARKED-UP VERSION OF THE SPECIFICATION

Please delete the paragraph at page 19, lines 17-21, and replace it with the following paragraph:

Figure 16 shows the alignment of leader and gag regions present in vectors pONY4Z **(SEQ ID NO: 63)**, 8Z **(SEQ ID NO: 64)** and ATG mutated 8Z **(SEQ ID NO: 65)** vector. The latter is referred to as pONY8ZA. The sequences aligned are from the NarI site in the leader to the Xba site between the EIAV gag sequence and the CMV promoter. Sequences in the leader are shown in italic and a space is present upstream of the position of the gag ATG; and

Atty. Dkt. No. 078883-0146

REMARKS

Applicants respectfully request that the foregoing amendments be made prior to examination of the present application. The amendments are made to correct multiple dependencies and do not change the scope of the invention.

Respectfully submitted,

By Reg No. 34,717

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MARKED UP VERSION OF AMENDED CLAIMS

3. (Once Amended) A method according to claim 1, [or claim 2] wherein the construct further comprises the 5'LTR and/or the packaging signal.

4. (Once Amended) A method according to [any one of claims] claim 1 [to 3], wherein the construct LTR is a heterologous regulatable LTR.

6. (Once Amended) A method according to [any one of claims] claim 1, [to 3] wherein the construct LTR is inactive.

7. (Once Amended) A method according to [any one of the preceding claims] claim 1, wherein the provirus comprises an NOI encoding a selectable marker, which NOI is flanked by recombianse recognition sites.

8. (Once Amended) A method according to [any one of the precedings claims] claim 1, wherein the provirus comprises an internal 5' LTR upstream of the recombinase site or the 5' recombinase site where there is more than one site.

10. (Once Amended) A method according to [any one of the preceding claims] claim 1, wherein the U3 region of the 5' LTR and/or the U3 region of the second internal 5' LTR comprises a heterologous promoter.

11. (Once Amended) A method according to [any one of the preceding claims] claim 1, wherein the provirus comprises two recombinase recognition sites and as a preliminary step, the recombinase is expressed in a host cell such that the nucleotide sequence present between the two sites is excised.

12. (Once Amended) A method according to [any one of the preceding claims] claim 1, wherein the producer cell is a high titre producer cell, capable of producing at least 10^6 retrovirus particles per ml.

13. (Once Amended) A method according to [any one of the preceding claims] claim 1, wherein the provirus is a lentivirus.

15. (Once Amended) A method according to [any one of claims] claim 2 [- 14], wherein the provirus further comprises a second NOI.

16. (Once Amended) A producer cell obtainable by the method of [any one of claims] claim 1 [to 15].

22. (Once Amended) A producer cell according to [any one of claims] claim 18, [to 21] wherein the third LTR is transcriptionally quiscent.

24. (Once Amended) A producer cell according to [any one of claims] claim 20, [to 23] wherein the first NOI is a selectable marker.

26. (Once Amended) A producer cell according to claim 25, wherein the second LTR comprises a deletion in the U3 sequences in the 3' LTR.

27. (Once Amended) A producer cell according to claim 25 [or claim 26], wherein the second NOI comprises a coding sequence operably linked to a promotor.

30. (Once Amended) A method for producing a high titre regulatable retroviral vector, the method comprising [the steps of]:

(i) providing a derived producer cell comprising integrated into its genome a first vector;

(ii) introducing a second vector into the derived producer cell using a recombinase assisted method;

wherein the derived producer cell comprises a retroviral vector comprising in the 5' to 3' direction a first LTR (5' LTR); a second NOI operably linked to a second LTR (regulatable

3' LTR); and a third LTR (3' LTR); wherein the third LTR is positioned downstream of the second LTR in the derived producer cell.

34. (Once Amended) A process for preparing a regulated retroviral vector, [as defined in claim 17] comprising performing the method according to [any one of claims] claim 30 [to 33] and preparing a quantity of the regulated retroviral vector.

38. (Once Amended) A regulated retroviral vector according to claim 36, [or claim 37] wherein the target site is a cell.

40. (Once Amended) [Use of a] A regulated retroviral vector according to [any one of claims] claim 35, [to 38] in [the manufacture of a pharmaceutical composition to deliver an NOI to a target site] combination with a pharmaceutically acceptable carrier.

41. (Once Amended) [Use of a regulated retroviral vector according to any one of claims 35 to 38 in the manufacture of a] A medicament for diagnostic and/or therapeutic and/or medical applications , comprising a regulated retroviral vector according to claim 35.

43. (Once Amended) A derived stable producer cell capable of expressing regulated retroviral vectors according to claim[s] 35 to [38].

47. (Once Amended) A nucleic acid vector according to claim 45, [or claim 46] further comprising a 5' LTR and/or a packaging signal.

48. (Once Amended) A nucleic acid vector according to [any one of claims] claim 45, [to 47] wherein the LTR is a heterologous regulatable LTR.

49. (Once Amended) A nucleic acid vector according to [any one of claims] claim 45, [to 47] wherein the LTR is transcriptionally quiscent.